Supplemental Materials

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Validation and Calibration for IMPACT CKD Model

Uncertainty in these models is a product of bias, simplification errors, and knowledge gaps that variably impacts the ability of model structures to replicate disease (i.e., the model health states are a simplification of a complex disease and may introduce unknown bias). As an example of simplification error in the present analysis, the IMPACT model used CKD stages such that costs and event risks progressed in a step wise manner. In reality, CKD progresses gradually and continuously with risk of events and costs varying within CKD states as well as between states. Further simplifications were made in limiting the number and types of patient characteristics and comorbidities considered, as the model is comprehensive but does not account for burdens such as obesity, smoking, etc. The data inputs used also introduced several potential sources of error such as; population sampling (i.e., study sample may not fully reflect country population), uncertainty due to reporting variability (i.e., data may not be uniformly reported or have differences in outcome definition), measurement error in the design and conduct of the study collecting the data, random error (i.e., studies may be underpowered to provide a robust estimate), and inconsistency introduced by data combination (i.e., data from multiple studies with varying populations, methodology, year of study were used). Due to this, using and combining input data without calibration was unlikely to produce model results that provide an accurate reflection of the population of interest.

For the IMPACT CKD model, four validation steps were used to assess and improve model validity. The model structure underwent tests of face validity with clinical experts in each country where an analysis was performed during the development phase. Verification or technical validation included review by an external programmer, coding walk throughs, and extreme value testing. Cross-validation was conducted versus the Inside CKD model built by Tangri and team, a patient-level microsimulation built in 2022 to project the epidemiological and economic impacts of CKD up to five years,[8] and the UK Kidney Research model, a population-level Markov model to investigate the kidney disease landscape in UK from 2023 to 2033.[3] Finally, calibration of select model inputs for the UK case study was conducted within a plausible range to align model outcomes with the validation targets (**Supplemental Table S36**). The calibration process involved an iterative process of adjusting inputs values (e.g., HR for CV events by CKD stage) within clinically plausible ranges to match validation targets (e.g. numbers of patients on dialysis). Prioritization of validation targets was reflected in the order of the parameters in **Supplemental Table S36**.

IMPACT CKD was aligned with the UK Kidney Research unconstrained projections for the number of patients on dialysis at year five and within the range of unconstrained and constrained projections for patients receiving a new transplant at year 10. In both models, 10-year growth was driven by assumptions regarding the rate of kidney transplantation. IMPACT CKD used current incident rates of transplantation and dialysis per million population with growth in incident transplantation consistent with growth in the general population (to model change in organ availability), and growth in incident dialysis consistent with changes in historical rates. In contrast, the UK Kidney Research model assumed constrained or unconstrained growth in transplantation and dialysis. The true number of transplants and new dialysis cases in future years will be contingent on supply of organs and access to dialysis, and as such is uncertain. However, the growth in dialysis patients projected by the IMPACT CKD model (18% over eight years) is supported by historical data on dialysis growth from the UK Renal Registry (15% over eight years). Inside CKD reported lower rates of growth of dialysis and transplantation.

Model Inputs

Supplemental Table S1: CKD stage as defined by eGFR and UACR

eGFR	UACR (mg/g)		
	<30	***30-300***	***>300***
<15	5	5	5
15-29	4	4	4
30-44	3b	3b	3b
45-59	3a	3a	3a
60-89	No CKD	2	2
≥90	No CKD	1	1

Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular infiltration rate; KDIGO = Kidney Disease Improving Global Outcomes; NICE = National Institute for Health and Care Excellence; UACR = urinary albumin creatinine ratio.
Source: KDIGO and NICE guidelines[17,18]

Supplemental Table S2: eGFR equations for CKD progressors

Variable	Beta Coefficient	
	Fast progressors	***General progressors***
Intercept	***-5.5996756***	***1.755951074***
Age at study index	0.014943805	-0.02402287
Sex: male (vs. female)	-0.11722897	-0.09556822
Heart failure diagnosis (yes vs. no)	-0.48923154	0.113886703
Hypertension diagnosis (yes vs. no)	0.129370109	0.039749304
Myocardial infarction prior diagnosis (yes vs. no)	0.091076059	0.020328179
Stroke prior diagnosis (yes vs. no)	0.02648745	0.067249773
Diabetes diagnosis (yes vs. no)	-0.56161103	0.340769213
eGFR (per unit higher)	-0.02916478	-0.00693121
UACR (per unit higher)	-0.00059024	-0.00025429

Abbreviations: CKD = Chronic kidney disease; eGFR = estimated glomerular filtration rate; UACR = urine albumin creatinine ratio.
Source: DISCOVER CKD[11,24]

Supplemental Table S3: Key Model Assumptions

Category	Assumption
Population and disease projections	The 10-year projections assumed that policies and funding allow a growth rate in dialysis and transplant availability as per historical trends. Transplant growth (1% per year) was based on country population growth assumed to reflect the number of organs available. Dialysis growth was based on historical data for number of patients initiating dialysis (3% per year). Notably, these constraints will be tested in future policy analyses.
	Interdependence of patient characteristics was not considered due to a lack of comprehensive data that would inform a correlation matrix for all patient characteristics.
	eGFR and albuminuria values were not adjusted for comorbidities due to limitations in the available data.
	Hypothetical individuals entering the model due to births or immigration did not have CKD and would not develop CKD within the 10-year time horizon. This is a simplifying assumption reflecting the low rates in those populations.
Clinical events	Due to a lack of comprehensive data in patients with CKD, the model did not consider the impact of patient characteristics (except CKD stage), including comorbidities, on the incidence of a clinical event. Instead, rates for patients with CKD were estimated using rates of events were for the general population adjusted by a hazard ratio for each event by CKD stage.
	Patients could only have one of each type of event per cycle. This is a simplifying assumption.
	Clinical events for patients living with a kidney transplant or on dialysis were not simulated.
	Conservatively, the occurrence of a hospitalization due to a HF event was only assigned in patients with HF.
Discounting	Costs and QALYs were not discounted or adjusted for inflation.
Transplantation	The model did not differentiate between types of transplants (i.e., living donor, deceased donor, grafts) instead using average data for costs and survival.
	The probability of primary transplant graft failure and subsequent graft failure was not captured in the model (ie., transplants were assumed to last for the entire time horizon).
Environmental impacts of CKD	The environmental inputs used in the analyses were associated to patients with CKD. However, the environmental impact may not be specific to CKD. For example, a patient with CKD stage 2 may also have another comorbidity, such as diabetes or hypertension, that may increase their water consumption, fossil fuel depletion, and carbon production. As such, for some patients CKD may contribute to a small proportion of the total impact. Because of this, care should be taken when projecting the incremental impact of reducing CKD occurrence or progression.

Category	Assumption
Validation	The model assumed that validation targets are representative of the country population; however, the validation targets have uncertainty due to data collection methods.

Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HF = heart failure; QALY = quality-adjusted life year; UK = United Kingdom.

Supplemental Table S4: Validation targets and input parameters subject to calibration

Validation Target	Contributing Model Input	Rationale
Baseline CKD stage distribution	eGFR value distribution and albuminuria value distribution by age and sex in the population	The data for eGFR and albuminuria distribution were often derived from studies with small sample size, or potential sample bias due to convenience sampling (e.g., populations with CKD, elderly populations, patients undergoing medical care). CKD stage distribution is a key model driver.
Prevalence of dialysis patients and growth rate over time	Eligibility criteria (probability of initiating dialysis by eGFR thresholds, willingness to initiate dialysis by age), rate of eGFR decline in fast and slow progressors, proportion of fast progressors, baseline dialysis population	Calibrated due to number of contributing inputs and to produce a baseline dialysis population and a growth rate that matched historical population data. This assumes that policies and funding will allow a growth rate in dialysis availability as per historical trends.
Prevalence of patients living with a kidney transplant and growth rate over time	Eligibility criteria (age threshold, eGFR threshold), probability of receiving transplant if eligible, rate of eGFR decline in fast and slow progressors, proportion of fast progressors, baseline transplant population	Calibrated due to number of contributing inputs and to produce a baseline transplant population and a growth rate that matched historical population data. This assumes that policies and funding will allow a growth rate transplant availability as per historical trends.
Probability of death in the total population (with and without CKD)	Mortality event rates due to stroke, MI, AKI, and kidney transplant Annual rates of death for patients living with dialysis, kidney transplant, HF, or CKD not treated with RRT and general population mortality	Calibrated due to number of contributing inputs and to avoid double counting as general population mortality and CKD stage mortality would include the influence of CV, AKI events, HF, dialysis, and transplant.
Incidence of MI, stroke, and hospitalization due to HF per million population (with and without CKD)	Annual probability by age and sex for general population, HR for increased risk by CKD stage	Calibrated to align with country-specific annual event estimates and due to number of contributing inputs and to avoid double counting as general population rate would include patients with CKD.

Validation Target	Contributing Model Input	Rationale
Incidence of AKI events per million population (with and without CKD)	Annual probability by age and sex for general population, HR for increased risk by CKD stage	Calibrated to produce an AKI event incidence that was reasonable and aligned with country specific estimates. AKI data in general were expected to have high uncertainty due to variability in documenting AKI events in clinics and a limited number of studies to utilize.
Incidence of HF cases per million population (with and without CKD)	Annual probability by age and sex for general population, HR for increased risk by CKD stage	Calibrated to align with country-specific annual event estimates and due to number of contributing inputs and to avoid double counting as general population rate would include patients with CKD.
Baseline prevalence of hypertension, stroke, MI, HF, diabetes among all patients (with and without CKD)	Prevalence rate by age and sex, prevalence rate by CKD stage	Calibrated to avoid double counting as general population rate would include patients with CKD.
CKD Growth	Non-CKD annual eGFR decline rate	Calibrated within a range from the literature to ensure growth of CKD at an acceptable rate.
Dialysis and transplant survival at years 1, 5, and 10	Dialysis and transplant mortality rates in year 1 and subsequent years	Calibrated as mortality rates for each country are not readily available; however, long-term survival data is often captured. This model input was calibrated to match the survival data of each country.

Abbreviations: AKI = acute kidney injury; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; HF = heart failure; HR = hazard ratio; MI = myocardial infarction; RRT = renal replacement therapy.

Supplemental Table S5: Kidney transplantation model inputs

Parameter	Value	Source
Age eligibility threshold (years)[a]	75	Expert opinion
eGFR eligibility threshold (mL/min/1.73 m^2)	10	Expert opinion
Percentage of eligible patients receiving transplant		
Percentage of incident RRT patients who receive a transplant	5.9%	UK Renal Registry, 2022[15]
Proportion of patients transitioning to transplant after dialysis[b, c]		
HD – year 1	5.6%	UK Renal Registry, 2022[15]
HD – subsequent years	3.18%	
PD – year 1	14.7%	
PD – subsequent years	6.10%	

[a]No transplant at or above age threshold. All patients above threshold receive palliative care.
[b]Subsequent year transition rate was calculated using Year 1 and year 5 rates.
[c]Proportion of patients transitioning to transplant for patients on HD was used for both home- and clinic-based HD.
Abbreviations: eGFR = estimated glomerular filtration rate; HD = hemodialysis; PD = peritoneal dialysis; RRT = renal replacement therapy; UK = United Kingdom.

Supplemental Table S6: Dialysis model inputs – Percentage of eligible patients by eGFR

Parameter	Value	Source
Probability of dialysis		
15-19 mL/min/1.73m^2	0%	Expert opinion
10-14 mL/min/1.73m^2	75%	
5-9 mL/min/1.73m^2	100%	KDIGO 2019[S1, a]; UK Renal Registry 2022[15, b]
<5 mL/min/1.73m^2	100%	As per above
Probability of modality		
In-center HD	77%	UK Renal Registry, 2022[15, c]
PD	23%	

[a]A specified eGFR value for initiation dialysis has not been established (usually based on symptoms); often between 5-10.
[b]Geometric mean eGFR at initiation is 7.10 (6.99-7.22) for HD; 7.43 (7.21-7.64) for PD; 10 (9.56-10.5) for transplant.
[c]Calculated from incident dialysis patients
Abbreviations: eGFR = estimated glomerular filtration rate; HD = hemodialysis; KDIGO = Kidney Disease: Improving Global Outcomes; PD = peritoneal dialysis; UK = United Kingdom.

Supplemental Table S7: Dialysis model inputs – Percentage of eligible patients that receive conventional kidney supportive care by age and eGFR

	eGFR (mL/min/1.73 m^2)			
Age (Years)	**<5**	**5-9**	**10-14**	**15-19**
<70	5.0	5.0	5.0	5.0
70-74	20.0	20.0	20.0	20.0
75-79	40.0	40.0	40.0	40.0
80-84	50.0	50.0	50.0	50.0
85+	70.0	70.0	70.0	70.0

Abbreviations: eGFR = estimated glomerular filtration rate.
Source: Clinical expert opinion.

Supplemental Table S8: Event risk – Annual probabilities of MI for the general UK population by age and sex

Age group	Male (per 100,000)	Female (per 100,000)
0-44 years	-	-
45-54 years	167.0	52.9
55-64 years	321.3	95.8
65-74 years	359.5	155.0
75+ years	587.4	340.7

Abbreviations: MI = myocardial infarction; UK = United Kingdom.
Source: British Heart Foundation, 2020[20]

Supplemental Table S9: Event risk – Annual probabilities of stroke/TIA for the general UK population by age and sex

Age group	Male (per 100,000)	Female (per 100,000)
0-44 years	-	-
45-54 years	157.8	119.5
55-64 years	325.9	235.4
65-74 years	665.3	466.1
75+ years	1 385.3	1 275.8

Abbreviations: TIA = transient ischemic attack; UK = United Kingdom.
Source: British Heart Foundation, 2020[20]

Supplemental Table S10: Event risk – Annual probabilities of AKI for the general UK population by age

Age (years)	Incidence rates (per 10,000 PY) Grampian, UK
18-29	28.5
30-39	40.8
40-49	41.6
50-59	80.8
60-69	179
70-79	369
≥80	773

Abbreviations: AKI = acute kidney injury; PY = patient-year; UK = United Kingdom.
Source: Sawhney et al., 2022[S2]

Supplemental Table S11: Event risk – Annual probabilities of HF resulting in hospitalization for the general UK population by age

Characteristic	Rate per 100 PY
Age <70	14.1
Age 70-79	18.1
Age 80-89	26.9
Age ≥90	35.2

Abbreviations: HF = heart failure; PY = patient-year; UK = United Kingdom.
Source: Lawson et al., 2019[S3]

Supplemental Table S12: Event risk – CKD-specific relative risk of MI by CKD stage and age

CKD Stage	Relative Risk	95% CI
Aged 20-64 years		
1	1.19	0.64 – 2.22
2	1.19	0.64 – 2.22
3	2.06	1.48 – 2.87
4	2.06	1.48 – 2.87
5	2.06	1.48 – 2.87
Aged 65+ years		
1	1.01	0.83 – 1.23
2	1.01	0.83 – 1.23
3	1.38	1.26 – 1.51
4	1.38	1.26 – 1.51
5	1.38	1.26 – 1.51

Abbreviations: CI = confidence interval; CKD = chronic kidney disease; MI = myocardial infarction; US = United States.
Source: U.S. Renal Data System.[S4]

Supplemental Table S13: Event risk – CKD-specific hazard ratios for incidence of stroke by eGFR and UACR status

eGFR (ml/min/1.73m^2)	Normal albuminuria (< 30 mg/g)	Microalbuminuria (30-300 mg/g)	Macroalbuminuria (> 300mg/g)
>90	Reference	1.53	1.94
60-90	1.14	1.75	2.22
30-60	1.64	2.50	3.17
15-30	2.78	4.26	5.40
<15	2.78	4.26	5.40

Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; g = grams; mg = milligrams; UACR = urinary albumin-creatinine ratio.
Source: Masson et al., 2015[S5]

Supplemental Table S14: Event risk – CKD-specific relative risk of AKI by CKD stage and age

CKD Stage (eGFR, ml/min/1.73m^2)	Relative Risk
1 (>90)	-
2 (60-89)	eGFR 60 = 0.993
3a (45-59)	eGFR 45 = 1.14
3b (30-44)	eGFR 30 = 1.67
4 (15-29)	eGFR 15 = 5.49
5 (<15)	eGFR 15 = 5.49

Abbreviations: AKI = acute kidney injury; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate.
Source: Grams et al., 2015[S6]

Supplemental Table S15: Event risk – CKD-specific rate ratios of hospitalization due to HF by CKD category

CKD category	Rate Ratio
eGFR >45, UACR <300	1.0 (reference)
eGFR <45, UACR <300	2.3
eGFR >45, UACR >300	2.9
eGFR <45, UACR >300	3.0

Note: Model adjustments include age, sex, and race/ethnicity, diabetes, history of cardiovascular disease, use of lipid-lowering medications, smoking, systolic blood pressure, and body mass index, use of diuretics, ACE inhibitors/ARBs and β-blocker.
Abbreviations: ACE Angiotensin-converting enzyme; ARB = Angiotensin receptor blockers; eGFR = estimated glomerular filtration rate; HF = heart failure; UACR = urinary albumin creatinine ratio.
Source: Bansal et al., 2019[S7]

Supplemental Table S16: Event risk – Outcomes of AKI

Outcome	Proportion of patients	One-time eGFR decline reduction
Full recovery (defined as return to baseline serum creatinine)	43%	0
Partial recovery (defined as return to serum creatinine is within 1.5 times the baseline value)	30%	12.5%[a]
No recovery (defined as return to serum creatinine is above 1.5 times the baseline value)	27%	25%[b]

[a] As a conservative assumption using the RIFLE severity classification (i.e., increased creatinine of 1.5-fold is similar to a >25% eGFR decline), patients in partial recovery were assumed to have a one-time eGFR reduction of 12.5%.
[b] As a conservative assumption using the RIFLE severity classification (i.e., increased creatinine of 1.5-fold is similar to a >25% eGFR decline), patients who did not recover were assumed to have a one-time eGFR reduction of 25%.
Abbreviations: AKI = acute kidney injury; eGFR = estimated glomerular filtration rate; RIFLE = Risk, Injury, and Failure; and Loss; and End-stage kidney disease.
Source: Duarte et al., 2022[S8]

Supplemental Table S17: Relative risk of all-cause mortality by CKD Stage

eGFR (mL/min/1.73m^2)	Albumin excretion rate		
	A1: Normal to mild albuminuria (<30mg/24h)	A2: Microalbuminuria (30-300mg/24h)	A3: Macroalbuminuria (>300mg/24h)
≥90	Reference group	1.5	3.1
60-90	1.0	1.7	2.3
45-60	1.3	2.2	3.6
30-44	1.9	3.3	4.9
15-30	5.3	4.7	6.6
<15	5.3	4.7	6.6

Assumptions: RR for albumin excretion rate <10 in that figure are included as risks for A1 as these are the most conservative; eGFR 90-105 in that figure is taken as the reference group for G1 (eGFR>90); eGFR 15-30 in that figure is taken as the relative risk for G5 (eGFR<15).
Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; h = hours; mg = milligrams.
Source: Adapted from Levey et al, 2011.[S9]

Supplemental Table S18: Mortality – Probability of patient survival by transplant type

Events	Number of kidney transplants (2020)	1-year Survival	5-year Survival	10-year Survival
Deceased Donor	1 903	96%	88%	73%
Living Donor	586	99%	95%	86%

Source: UK Renal Registry, 2022[15]

Supplemental Table S19: Dialysis mortality – Probability of patient mortality by age

Age	1-year mortality	Subsequent years
0-34	1.84%	4.18%
35-44	4.14%	
45-54	6.90%	6.33%
55-64	11.04%	8.51%
65-74	16.10%	9.89%
75-84	23.00%	11.27%
85+	29.90%	

Source: Moist et al., 2014;[S10] Robinson et al., 2013[S11]

Supplemental Table S20: Mortality – Probability of patient mortality from clinical events

Events	Rates (Men)	Rates (Women)	Source
MI	25.4%	24%	Asaria et al., 2022[S12, a]
Stroke	15%	15%	British Heart Foundation, 2021[20]
AKI	17.02%	17.02%	Think Kidneys 2018[S13, b]
HF	22.1%	24.6%	Taylor 2020[S14, c]

[a] Based on a large, retrospective study using linked data from national databases on hospitalizations and deaths with MI from 2015 to 2018.

[b] Calculated as an age- and sex- standardized 30-day mortality rate from AKI episodes from the last 12 months reported to the UK Renal Registry (2016-2017).

[c] Calculated as a one-year mortality rate. Based on a large, retrospective study using UK primary care data for 26,725 women and 29,234 men over age 45 with a new diagnosis of HF between 2001 and 2017 using the Clinical Practice Research Datalink, inpatient Hospital Episode Statistics and the Office for National Statistics death registry.

Abbreviations: AKI = acute kidney injury; HF = heart failure; MI = myocardial infarction; UK = United Kingdom.

Supplemental Table S21: Mortality rates (qx), males and females, UK, 2018-2020

Age (years)	Male	Female
0	0.004224	0.003503
1	0.000229	0.000214
2	0.000127	0.000114
3	0.000102	0.000095
4	0.000086	0.000064
5	0.000074	0.000074
6	0.000085	0.000071
7	0.000067	0.000055
8	0.000069	0.000058
9	0.00006	0.000051
10	0.000078	0.000066
11	0.000077	0.000055
12	0.000102	0.000057
13	0.000116	0.000087
14	0.000129	0.000096
15	0.000172	0.000113
16	0.000205	0.000131
17	0.000311	0.000158
18	0.000402	0.000218
19	0.000454	0.000212
20	0.000525	0.000187
21	0.000507	0.000211
22	0.000497	0.000245
23	0.000524	0.000215
24	0.000556	0.000223
25	0.000601	0.00026
26	0.000607	0.000257
27	0.000629	0.00031
28	0.000681	0.000314
29	0.000728	0.000338
30	0.000771	0.000387
31	0.000835	0.000394
32	0.000858	0.000468
33	0.000957	0.000493
34	0.000989	0.000585
35	0.0011	0.000592
36	0.001155	0.000678
37	0.001351	0.000761
38	0.001317	0.000792
39	0.001457	0.000868
40	0.001606	0.000924
41	0.0017	0.001004
42	0.001848	0.001102

Age (years)	Male	Female
43	0.002015	0.001239
44	0.00221	0.001345
45	0.002467	0.001484
46	0.002646	0.001625
47	0.002743	0.001744
48	0.00296	0.001966
49	0.003297	0.002051
50	0.003577	0.002234
51	0.003821	0.002452
52	0.004075	0.002581
53	0.004402	0.002764
54	0.00472	0.002964
55	0.005046	0.003283
56	0.005593	0.003637
57	0.00606	0.003928
58	0.006695	0.004367
59	0.007239	0.004707
60	0.007912	0.005247
61	0.008636	0.005636
62	0.009601	0.006451
63	0.010552	0.006818
64	0.011171	0.007379
65	0.01246	0.008113
66	0.013853	0.00877
67	0.014782	0.009554
68	0.016348	0.010602
69	0.017949	0.011458
70	0.019238	0.012895
71	0.020795	0.013637
72	0.022782	0.015499
73	0.025799	0.017289
74	0.028776	0.019688
75	0.0323	0.021766
76	0.03573	0.024397
77	0.040136	0.027918
78	0.045188	0.03142
79	0.050259	0.035713
80	0.056143	0.039611
81	0.06203	0.045127
82	0.069197	0.050197
83	0.077486	0.057155
84	0.087296	0.065142
85	0.097476	0.073748
86	0.110221	0.08452

Age (years)	Male	Female
87	0.122808	0.095918
88	0.137654	0.107798
89	0.154513	0.121609
90	0.163489	0.136466
91	0.183325	0.153438
92	0.200869	0.171026
93	0.222981	0.189568
94	0.244606	0.20787
95	0.268951	0.230227
96	0.290494	0.253171
97	0.31405	0.277939
98	0.335507	0.299649
99	0.369942	0.31991
100	0.390506	0.350742

Abbreviations: UK = United Kingdom.
Source: UK Office for National Statistics[14]

Supplemental Table S22: Comorbidities risk – Annual probabilities of T2DM for the general UK population by age

Age (years)	Males (per 100,000)	Females (per 100,000)
16-24	2.1	1.0
25-34	8.3	6.22
35-44	23.7	14.5
45-54	51.5	33.3
55-64	80.4	54.1
65-74	88.7	61.4
75+	99.0	67.7

Abbreviations: T2DM = type 2 diabetes mellitus; UK = United Kingdom.
Source: Zghebi et al., 2017[S15]

Supplemental Table S23: Comorbidities risk – Annual probabilities of HTN for the general UK population by age and sex

Age	Male (2-year incidence, per 100)	Female (2-year incidence, per 100)
30-39	3.32	1.44
40-49	4.46	3.59
50-59	4.72	5.01
60-69	5.66	6.92
70-79	6.25	8.61

Abbreviations: HF = heart failure; HTN = hypertension; UK = United Kingdom.
Source: Framingham Study, Dannenberg 1988.[S16]

Supplemental Table S24: Comorbidities risk – Annual probabilities of HF for the general UK population by age and sex

Age (years)	Male (per 100,000)	Female (per 100,000)
45-54	64.5	32.3
55-64	161.6	71.9
65-75	353.9	197.3
75+	1 182.2	801.6

Abbreviations: HF = heart failure; UK = United Kingdom.
Source: British Heart Foundation, 2020[20]

Supplemental Table S25: Comorbidities risk – CKD-specific relative risk of T2DM by CKD stage and age

CKD Stage (eGFR, mL/min/1.73m^2)	Relative Risk
1 (>90)	1.24
2 (60-89)	1.24
3a (45-59)	1.24
3b (30-44)	1.24
4 (15-29)	1.24
5 (<15)	1.24

Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HR = hazard ratio; T2DM = type 2 diabetes mellitus; UK = United Kingdom.
Note: HR of developing diabetes in overall CKD is 1.24
Source: Lin 2019[S17]

Supplemental Table S26: Comorbidities risk – CKD-specific relative risk of HF by CKD stage and age

CKD Stage	Relative Risk	95% CI
Aged 20-64 years		
1	1.49	1.14 -1.95
2	1.49	1.14 -1.95
3	2.96	2.56 – 3.41
4	2.96	2.56 – 3.41
5	2.96	2.56 – 3.41
Aged 65+ years		
1	1.45	1.33 – 1.68
2	1.45	1.33 – 1.68
3	1.68	1.61 – 1.75
4	1.68	1.61 – 1.75
5	1.68	1.61 – 1.75

Abbreviations: CI = confidence interval; CKD = chronic kidney disease; HF = heart failure.
Source: U.S. Renal Data System 2009[S4]

Supplemental Table S27: Comorbidities risk – CKD-specific relative risk of HTN by CKD stage and age

CKD Stage (eGFR, mL/min/1.73m^2)	Relative Risk
1 (>90)	1.33
2 (60-89)	1.33
3a (45-59)	1.33
3b (30-44)	1.33
4 (15-29)	1.33
5 (<15)	1.33

Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HTN = hypertension.
Source: Hounkpatin et al., 2020[S18]

Supplemental Table S28: Annual resource burden associated with CKD

CKD Stage/Treatment modality	ER visits per year	Hospitalizations per year	Outpatient visits per year
Stage 1	0	0	0
Stage 2	0.304246	0.495608	2.678467
Stage 3a	0.332568	0.544815	2.770741
Stage 3b	0.450719	0.688983	3.076986
Stage 4	0.553543	0.947778	4.039855
Stage 5	0.834935	2.449808	9.987087
Stage 5, Transplant	0.834935	2.449808	9.987087
Stage 5, Dialysis	0.834935	2.449808	9.987087

Abbreviations: CKD = chronic kidney disease; ER = emergency room.
Source: DISCOVER CKD[11]

Supplemental Table S29: Annual per patient costs associated with treatment of CKD by stage and treatment modality

Condition	Annual cost (£, 2022)	Source
CKD-related costs by stage		
CKD Stage 1	Assumed 0	-
CKD Stage 2	Assumed 0	-
CKD Stage 3a	851	AstraZeneca 2021 (DAPA-CKD);[S19] McEwan 2022[S20]
CKD Stage 3b	959	
CKD Stage 4	1 252	
CKD Stage 5 (pre-RRT)	2 071	
CKD Stage 5 (conservative care)	5 620	Kerr 2016[S21]
RRT-related costs		
Hemodialysis	24 689	NHS England and NHS Improvement, 2020[S22]
Peritoneal Dialysis	29 061	
Transplant	28 775	NHS Improvement, 2019[S23]
Transplant Maintenance	6 369	NHS Blood and Transplant, 2017[S24]
Event-related costs		
MI	6 027	Danese et al., 2016[S25]
Stroke	2 802	Luengo-Fernandez et al., 2020[S26]
AKI	5 286	Kolhe et al., 2014[S27]
Hospitalization for HF	6 091	Osenenko et al., 2022[S28]

Abbreviations: AKI = acute kidney injury; CKD = chronic kidney disease; DAPA-CKD = Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease; MI = myocardial infarction; NHS = National Health Service; RRT = renal replacement therapy.

Supplemental Table S30: Health state utility inputs and event-related disutility

Condition	Utility	Source
CKD-related health state utility		
CKD Stage 1	0.850	Assumed same as CKD Stage 2
CKD Stage 2	0.850	Cooper et al., 2020[S29]
CKD Stage 3a	0.730	
CKD Stage 3b	0.730	
CKD Stage 4	0.740	
CKD Stage 5 (pre-RRT)	0.740	
Peritoneal Dialysis	0.570	
Hemodialysis	0.670	
Post-transplant	0.830	
Event-related disutilities		
MI (non-fatal)	-0.087	AstraZeneca 2021 (DAPA-CKD);[S19] McEwan 2022[S20]
Stroke	-0.0524	Sullivan et al., 2006[S30]
AKI	-0.07825	Perera et al., 2021[S31]
Hospitalization for HF	-0.076	Luca DiTanna 2021[S32]

Abbreviations: AKI = acute kidney injury; CKD = chronic kidney disease; DAPA-CKD = Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease; MI = myocardial infarction; NHS = National Health Service; RRT = renal replacement therapy

Supplemental Table S31: Absenteeism and presenteeism in patients with CKD

CKD stage, treatment modality	Absenteeism (Days per year)		Presenteeism (Days per year)	
	Mean	*SD*	*Mean*	*SD*
No CKD	-	-	-	-
Stage 1	-	-	-	-
Stage 2	-	-	-	-
Stage 3a	17.04	47.76	45.12	47.52
Stage 3b	12.24	35.52	47.04	45.36
Stage 4	19.92	47.76	66.96	53.52
Stage 5	30.24	55.2	51.12	57.36
Stage 5, Transplant	11.04	47.04	36.0	49.92
Stage 5, Hemodialysis	29.28	57.6	83.28	59.28
Stage 5, Peritoneal Dialysis	29.28	57.6	83.28	59.28

Abbreviations: CKD = chronic kidney disease; SD = standard deviation

Source: van Haalen et al., 2020[S33]

Supplemental Table S32: Absenteeism in caregivers of patients with CKD

CKD stage, treatment modality	Absenteeism (Days per year)	
	Mean	*SD*
Stage 1	3.1	18.2
Stage 2	3.1	18.2
Stage 3a	3.1	18.2
Stage 3b	3.1	18.2
Stage 4	27.0	84.6
Stage 5	27.0	84.6
Stage 5, Transplant	11	31
Stage 5, Hemodialysis	104.8	325.1
Stage 5, Peritoneal Dialysis	104.8	325.1

Abbreviations: CKD = chronic kidney disease; SD = standard deviation
Source: Eriksson, 2017[S34]

Supplemental Table S33: Productivity inputs

Input	Value	Source
Cost per workday	£134	Office for National Statistics 2022[S35]
UK purchase power parity	103	OECD 2022[S36]
Percent of absenteeism considered as sick-pay disbursement	50%	Assumption
Percent of absenteeism considered as lost tax revenue	50%	Assumption
Average tax rate for UK worker	35%	OECD 2023[S37]

Abbreviations: OECD = Organization for Economic Co-operation and Development; SD = standard deviation; UK = United Kingdom.

Supplemental Table S34: Annual per patient environmental burden associated with CKD

CKD stage, treatment modality	Climate change (kg CO_2 eq.)	Fossil depletion (kg oil eq.)	Freshwater Consumption (m^3)
Stage 1	445	193	2
Stage 2	482	212	2
Stage 3	610	272	3
Stage 4	841	377	4
Stage 5, conservative care	1 270	575	6
Stage 5, dialysis	4 950	2 200	46
Stage 5, transplant	2 620	1 110	19
Stage 5, transplant maintenance	918	410	4

Abbreviations: CKD = chronic kidney disease; CO_2 = carbon dioxide; eq. = equivalents; kg = kilograms.
Source: AstraZeneca Data on File[S38]; Zoccali et al. 2023[12]

Supplemental Table S35: Lifestyle and Financial burden associated with CKD

CKD Stage	% of Work Time Missed	% of Impairment in Daily Activities	CFPB Score	FACIT-Cost Score
Stage 1	31.4%	47.1%	51.89	26.54
Stage 2	31.4%	47.1%	51.89	26.54
Stage 3a	31.4%	47.1%	51.89	26.54
Stage 3b	31.4%	47.1%	51.89	26.54
Stage 4	31.4%	47.1%	51.89	26.54
Stage 5	31.4%	47.1%	51.89	26.54
Transplant	31.4%	47.1%	51.89	26.54
Transplant Maintenance	31.4%	47.1%	51.89	26.54
Hemodialysis	40.2%	58.6%	51.89	21.08
Peritoneal Dialysis	40.2%	58.6%	51.89	21.08

Abbreviations: CKD = chronic kidney disease; CFPB = Consumer Financial Protection Bureau; FACIT = Functional Assessment of Chronic Illness Therapy.
Source: AstraZeneca Data on File;[S39] PACE-CKD[13]

Validation and Calibration Targets

Supplemental Table S36: Targets for model calibration and external validation

Parameter	Validation Target (per million or as %)	Calibrated Model Output (per million or as %)	Validation Source
Baseline Characteristics			
% Female in Total Population	50.60	50.59	UK ONS[14]
Average age of Total Population (years)	40.30	40.61	
Proportion of patients with diabetes			
% of CKD Stage 1 patients with diabetes at baseline	18.48	18.41	USRDS 2022[S40]
% of CKD Stage 2 patients with diabetes at baseline	24.00	24.07	
% of CKD Stage 3a patients with diabetes at baseline	26.32	26.38	
% of CKD Stage 3b patients with diabetes at baseline	26.32	26.21	
% of CKD Stage 4 patients with diabetes at baseline	43.04	43.33	
% of CKD Stage 5 patients with diabetes at baseline	43.04	42.52	
Proportion of patients with hypertension			
% of CKD Stage 1 patients with hypertension at baseline	35.80	35.71	USRDS 2022[S40]
% of CKD Stage 2 patients with hypertension at baseline	48.10	48.01	
% of CKD Stage 3a patients with hypertension at baseline	59.90	59.94	
% of CKD Stage 3b patients with hypertension at baseline	59.90	59.85	
% of CKD Stage 4 patients with hypertension at baseline	84.10	84.29	
% of CKD Stage 5 patients with hypertension at baseline	84.10	84.49	
Proportion of patients with heart failure			
% of CKD Stage 1 patients with heart failure at baseline	4.40	4.37	USRDS 2022[S40]
% of CKD Stage 2 patients with heart failure at baseline	4.40	4.43	
% of CKD Stage 3a patients with heart failure at baseline	5.80	5.79	
% of CKD Stage 3b patients with heart failure at baseline	5.80	5.88	
% of CKD Stage 4 patients with heart failure at baseline	8.20	7.99	
% of CKD Stage 5 patients with heart failure at baseline	8.20	8.00	

Parameter	Validation Target (per million or as %)	Calibrated Model Output (per million or as %)	Validation Source
Proportion of patients with prior MI			
% of patients with CKD with prior MI at baseline (total)	NA	7.90	USRDS 2022[S40]
% of CKD Stage 1 patients with prior MI at baseline	7.80	7.74	
% of CKD Stage 2 patients with prior MI at baseline	7.80	7.83	
% of CKD Stage 3a patients with prior MI at baseline	7.80	7.85	
% of CKD Stage 3b patients with prior MI at baseline	7.80	7.81	
% of CKD Stage 4 patients with prior MI at baseline	11.40	10.70	
% of CKD Stage 5 patients with prior MI at baseline	11.40	10.93	
Proportion of patients with prior stroke			
% of patients with CKD with prior stroke at baseline (total)	NA	6.01	USRDS 2022[S40]
% of CKD Stage 1 patients with prior stroke at baseline	5.95	5.84	
% of CKD Stage 2 patients with prior stroke at baseline	5.95	5.97	
% of CKD Stage 3a patients with prior stroke at baseline	5.95	6.12	
% of CKD Stage 3b patients with prior stroke at baseline	5.95	6.09	
% of CKD Stage 4 patients with prior stroke at baseline	7.30	6.43	
% of CKD Stage 5 patients with prior stroke at baseline	7.30	6.89	
Proportion of patients with CKD in total population			
% of patients with CKD of total population at baseline	13.9%	12.35%	Hounkpatin 2020[S18]
	18.2%		Hirst 2020[5]
% of CKD Stage 1 patients of total population at baseline	3.99%	3.62%	HSE 2016[16]
% of CKD Stage 2 patients of total population at baseline	3.67%	3.45%	
% of CKD Stage 3a patients of total population at baseline	4.86%	2.46%	
% of CKD Stage 3b patients of total population at baseline		2.43%	
% of CKD Stage 4 patients of total population at baseline	0.2%	0.15%	
% of CKD Stage 5 patients of total population at baseline		0.24%	

Parameter	Validation Target (per million or as %)	Calibrated Model Output (per million or as %)	Validation Source
Proportion of patients with CKD by stage			
% of CKD Stage 1 patients at baseline	31.30%	29.29%	HSE 2016[16]
% of CKD Stage 2 patients at baseline	28.80%	27.95%	
% of CKD Stage 3a patients at baseline	38.20%	19.90%	
% of CKD Stage 3b patients at baseline		19.69%	
% of CKD Stage 4 patients at baseline	1.60%	1.20%	
% of CKD Stage 5 patients at baseline		1.96%	

Abbreviations: CKD = chronic kidney disease; HSE = Health Survey of England; MI = myocardial infarction; ONS = Office for National Statistics; USRDS = United States Renal Database System; UK = United Kingdom.

UK Case Study Results

Supplemental Table S37: IMPACT CKD predictions for change from baseline (2022) to 2032 for clinical, economic, patient, societal, and environmental burdens

Category	2022	2032	Percent Change
Number of people in UK	67 000 000	70 455 459	5.2%
CKD prevalence			
Number of patients with CKD	8 274 768	8 910 196	7.7%
Number of patients with CKD stage 3-5 (including dialysis)	3 538 069	4 304 750	21.7%
Number of patients with diagnosed CKD	2 394 915	2 968 636	24.0%
RRT prevalence			
Number of patients receiving RRT	73 365	121 940	66.2%
Number of patients undergoing dialysis	33 098	58 022	75.3%
Number of post-transplant patients	40 267	63 918	58.7%
Cost of CKD			
Annual cost of CKD[a]	£1.90 B	£2.45 B	29.6%
Annual cost of CKD stage 3	£1.52 B	£1.80 B	18.6%
Cost of RRT			
Annual cost of RRT	£1.09 B	£1.95 B	78.0%
Annual cost of dialysis	£0.84 B	£1.47 B	75.0%
Annual cost of transplant	£0.26 B	£0.48 B	88.0%
Patient burden			
Cumulative lost income (over 10 years)	-	£49 B	-
Societal burden			
Cumulative missed workdays for patients with CKD and caregivers (over 10 years)	-	362 M	-
Lost FTEs (over 10 years)	-	1.8 M	-

Category	2022	2032	Percent Change
Environmental burden			
Freshwater consumption (m^3)	1 697 846	2 998 381	76.6%
Fossil fuel depletion (kg oil eq.)	89 325 070	156 199 780	74.9%
Overall carbon footprint (kg CO_2 eq.)	200 800,206	351 587 324	75.1%

[a] Excludes costs associated with RRT.

Abbreviations: CKD = chronic kidney disease; eq. = equivalent; FTE = full-time equivalent; RRT = renal replacement therapy; UK = United Kingdom.

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